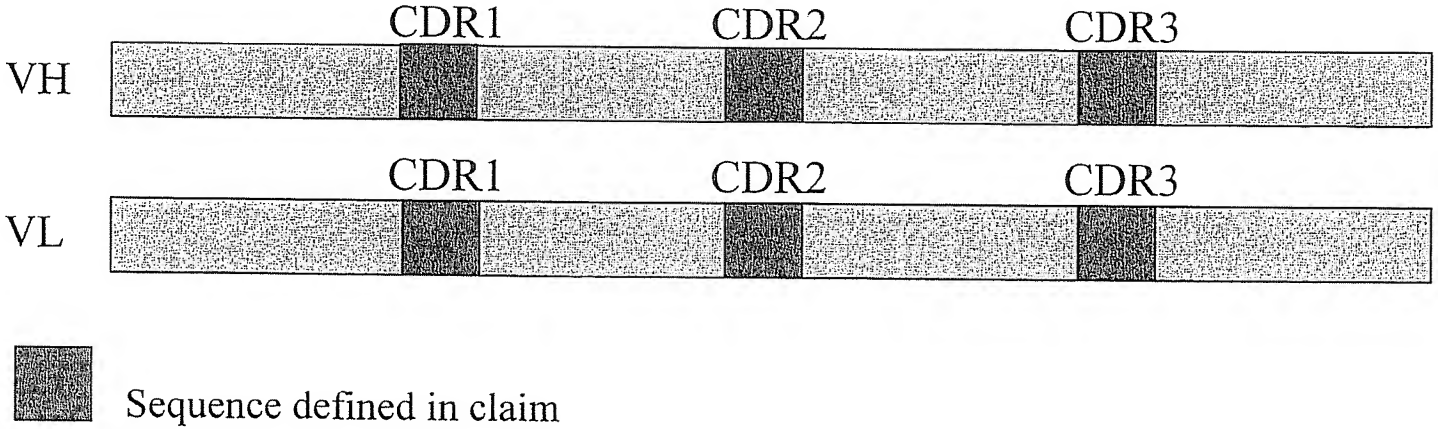
APPENDIX A

Example 1

- Claim: An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain comprising the 3 CDRs in SEQ ID NO:1 and a light chain variable domain comprising the 3 CDRs in SEQ ID NO:2.



Specification

- Discloses antigen X from human tissue.
- Discloses antigen X is over-expressed in cancer tissue vs. normal tissue.
- The instant application produced an antibody that binds antigen X that contains a VH of SEQ ID NO:1 and a VL of SEQ ID NO:2, as well as explicitly disclosing humanized and chimaeric antibodies.
- The instant application provides examples of detection of cancer in human subjects with an antibody that binds antigen X.

State of the Prior Art

- It was well known at the time the application was filed that the heavy and light polypeptide chains each contribute three CDRs to the antigen binding region of the antibody molecule.
- The prior art[1] taught humanization of antibodies by transfer of the 6 CDRs from a donor framework region to an acceptor framework region and retention of antigen binding.

[1]Queen et al., PNAS (1988) 86:10029-10033,
Riechmann et al., Nature (1988) 332:323-327

Analysis

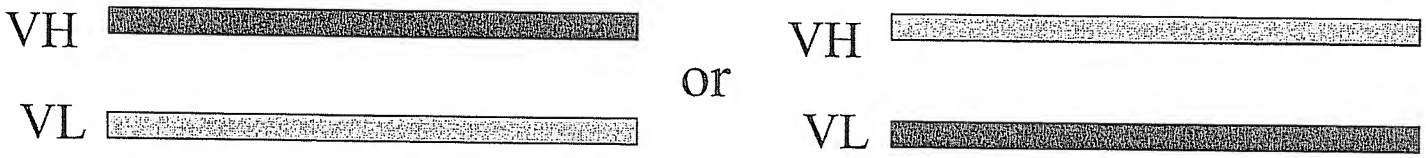
- In light of the prior art disclosing the CDRs as being the essential structure of the antibody's binding site, the identification of the specific CDR sequences in the specification provides enough structure to define the antibody's binding site.
- In addition, the prior art for humanization supports obtaining successful antigen binding by transferring the 6 CDRs from a donor framework to an acceptor framework.

Analysis (cont.)

- Thus, it would not have been undue experimentation to obtain an antibody that would bind antigen X and comprise the 6 CDRs as specifically defined in the claim at the time of filing.
- Therefore, a claim that defines an antibody that binds antigen X and comprises a heavy chain variable region comprising the 3 CDRs in SEQ ID NO:1 and a light chain variable region comprising the 3 CDRs in SEQ ID NO:2 meets the requirements under 35 U.S.C. 112, first paragraph, for enablement.

Example 2

- Claim 1. An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain comprising SEQ ID NO:1.
- Claim 2. An isolated antibody that binds to human antigen X, said antibody comprises a light chain variable domain comprising SEQ ID NO:2.



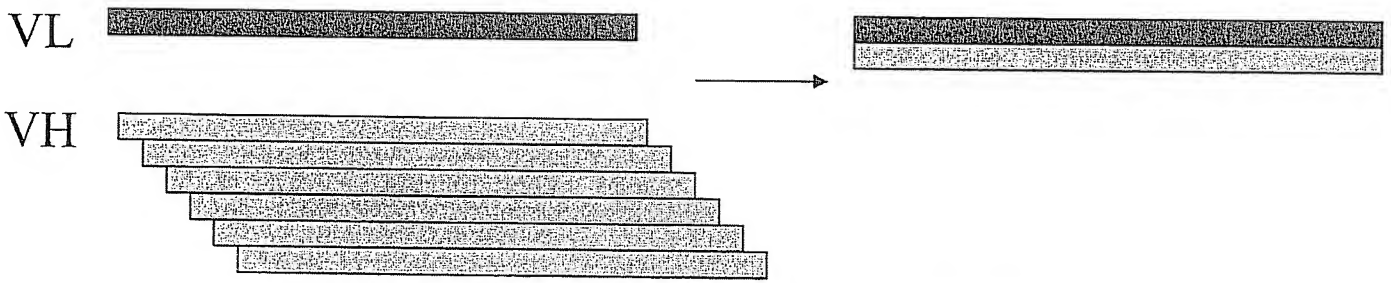
Sequence defined in claim

Specification

- Discloses antigen X from human tissue.
- Discloses antigen X is over-expressed in cancer tissue vs. normal tissue.
- The instant application produced an antibody that binds antigen X that contains a VH of SEQ ID NO:1 and a VL of SEQ ID NO:2, as well as explicitly disclosing humanized and chimaeric antibodies.
- The instant application provides examples of detection of cancer in human subjects with an antibody that binds antigen X.

State of the Prior Art

- There are several prior art[2] references that teach methods of producing antibodies that bind a specific antigen by using a specific VL (or VH) and screening a library of the complimentary variable domains.



[2]Portolano et al., The Journal of Immunology (1993) 150:880-887
Clarkson et al., Nature (1991) 352:624-628

Analysis

- In light of the prior art disclosing methods of obtaining antibodies that bind an antigen by screening complementary variable domain libraries, the specification's disclosure of an antibody that binds a specific antigen comprising a defined VH or VL sequence would provide enough structure for one skilled in the art to practice the invention.
- Therefore, claims directed to an antibody that binds a specific antigen and comprises a defined VH or VL sequence meet the requirements under 35 U.S.C. 112, first paragraph, for enablement.